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Original article

Central venous catheter related bloodstream infections in adult patients on home parenteral nutrition: Prevalence, predictive factors, therapeutic outcome

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SUMMARY

Background: The prevalence of central venous catheter (CVC)-related blood-stream infections (CRBSI), infecting agents and the effectiveness of antibiotic therapy were evaluated in 172 adult patients on Home Parenteral Nutrition (HPN) at the Clinical Nutrition Outpatient Unit of Federico II University Hospital in Naples, Italy.

Materials and methods: The study population consisted of 127 oncological (74%) and 45 (26%) non-oncological patients, for a total of 53,818 (median 104; range 14–1080) CVC days.

Results: Ninety-four CRBSIs were diagnosed on 238 CVC (infection rate 1.74/1000 CVC days). Coagulase negative (CoNs) Staphylococci were the most frequently infecting agents (52.8% as single agent) with 17.1% *Staphylococcus epidermidis* infections. Eighty-three percent *S. epidermidis* were beta-lattamase producer (BLACT), 66.6% methicillin-resistant (MR) and 55.5% had a MIC for Vancomicin $\geq$1. Gram-negative bacteria represented 18.6% infections, fungi 7.1%, finally 15% infections were polymicrobial. Previous catheterizations and the presence of an enterocutaneous stoma were significantly related with a higher infection risk ($p < 0.0001$ in both cases).

Conclusions: CRBSI and antibiotic resistance of infecting agents remain an important challenge in adult patients on HPN; an active research on strategies to counteract the phenomena is required.

1. Introduction

Parenteral nutrition (PN) is a lifesaving treatment for patients with chronic benign intestinal failure and an effective support for patients with gastrointestinal involvement by neoplastic diseases. Home PN (HPN) is now a well recognized and widely spread procedure which may be performed in the long-term, thus ameliorating patients' quality of life and reducing public health costs [1,2].

Central venous catheter (CVC)-related blood-stream infections (CRBSI) represent the most serious and common complication of long-term HPN and can contribute to patients' morbidity and mortality; they usually require hospital admission, with increasing costs for the healthcare system [3–5].

1.1. Aim of the study

The study aims: 1) to retrospectively evaluate CVC infection rate and the type of infectious agent determining CRBSI in a setting of oncological and non-oncological outpatients on HPN; 2) to evaluate possible predictive risk factors of CVC infection and effectiveness of antibiotic therapy.

2. Patient and methods

A retrospective, observational study on all consecutive patients receiving HPN from January 2010 to December 2012 at the Clinical

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Medicine and Surgery Department of Federico II University Hospital in Naples, Italy, was performed. Adult patients receiving HPN for less than 2 weeks and those receiving PN through a peripheral vein were excluded from the study.

2.1. Patients

Information about age, gender, underlying disease (oncological, non-oncological), implanted CVC type, number of CRBSI, infecting agent type, days of catheterization, infusion frequency, previous CVC infections, duration, modality of antibiotic treatment and clinical outcome were collected for each patient.

2.2. CRBSI diagnosis

CRBSI diagnosis was made according to the ESPEN and IDSA guidelines [6,7]. CRBSI is defined as isolation of the same microorganism from semi-quantitative or quantitative cultures of both blood drawn from the catheter lumen and the blood peripherally drawn of the patient with clinical symptoms of a bloodstream infection and no other apparent source of infection.

In some circumstances, in particular in terminal oncologic patients already followed by the oncologist and/or the medical practitioner, empiric antibiotic therapy was started before taking blood for culture. In these cases, when no other sources of infection were suspected, CRBSI diagnosis was performed according to hard clinical findings such as fever and shivering during catheter use, despite the negative/missing blood culture results.

Before HPN initiation, all patients and/or their caregivers received oral and written instructions by the clinical-nutrition team on CVC aseptic management and how to recognize both infectious and non-infectious complications [8,9].

2.3. Statistical analysis

The data obtained were analyzed with specific software for statistical analysis (SPSS 15.0). Results are expressed as mean, standard deviation and range. The *t*-test was used for comparison of unpaired data and χ^2 test for proportions. A logistic regression analyzed the correlation between variables. Multi-variate analysis was applied for risk factor evaluation. Differences among variables were considered statistically significant for p values <0.05.

3. Results

One hundred seventy two [91 (53%) M, 81 (47%) F] patients receiving HPN between January 2010 and December 2012 at the Clinical Nutrition Unit were evaluated.

The study population consisted of 127 (74%) oncological and 45 (26%) non-oncological adult patients, for a total of 53,818 days of catheterization and 49,254 days of HPN (Table 1). The type of disease in oncological and non-oncological patients is detailed in Table 2.

HPN frequency was 7 days per week in 151 (88%) patients, and 3–5 days per week in 21 (12%) patients.

In non-oncological patients, HPN generally began soon after CVC insertion (1 ± 2 days, min 0, max 10, median 1), whereas in oncological patients CVC generally was previously inserted for intravenous chemotherapy (CHT), even several months before beginning HPN (71 ± 108 days, 0–639, median 20.5). Twenty-four (14.5%) out of 172 patients had an enterocutaneous stoma.

A total of 238 CVC were inserted in 172 patients; the type of catheters inserted was detailed in Table 1. Forty-eight out of 172 (27.9%) patients had already undergone a previous catheterization. Globally, ninety-four CRBSIs were diagnosed on 238 inserted CVC, corresponding to an infection rate of 1.74/1000 CVC days.

In 70/94 (74.5%) cases blood cultures were positive. In 24/94 (25.5%) cases blood cultures were negative due to the starting of empiric antibiotic therapy before blood culture.

By focusing the attention only on the 70 infections with positive blood culture results (Table 3), in 55/70 (78.6%) cases the infection was due to a single infecting agent and in 15/70 (21.4%) to 2 or more germs: 4 with fungi, 9 with 2 infecting agents and 2 with 3 agents, in these last cases, fungi were always present.

Finally, 83.3% (15/18) isolated *S. epidermidis* were beta-lactamase producer, 66.6% (12/18) methicillin resistant and 66.6% (12/18) had a Minimal Inihibiting Concentration (MIC) for Vancomicine ≥1; 71.4% (5/7) *S. aureus* infections were methicillin-resistant (MRSA) with an elevated MIC for vancomicin.

3.1. Clinical outcome

In the 24/94 cases with negative cultures and hard clinical findings for CVC infection, the CVCs were promptly removed and empiric antibiotic therapy started.

As regards the 70 cases with positive blood results, 17 (24.3%) short-term CVCs were immediately removed; in 20/70 (28.6%) cases, according the current guidelines [13,14], the catheter was immediately removed for 9 fungal/polymicrobial infections, 7 S. aureus and 4 Gram negative (3 Pseudomonas, 1 Klebsiella pneumoniae) infections. As far as secondary complications, 3 S. aureus infections were complicated by septic pneumonia and 1 by septic endocarditis. Two infections by Gram negative bacteria were complicated by septic shock; 4 infections were associated with venous thrombosis.

Systemic and Local Antibiotic Therapy (Antibiotic Lock Therapy) were performed in the remaining 33/70 (41.14%) cases (Table 4), and in 22/33 (66.7%) cases the catheter salvage was successful.

Median antibiotic therapy length was 21 (range) 14–28 days according to the type of infection to treat.

A logistic regression model which considered previous catheterization, CVC use also for chemotherapy, type of catheter and the presence of a entero-cutaneous stoma as confounding variables, showed that a previous catheterization was significantly related with a higher infection risk ($p < 0.001$).

The number of infections per patient was positively related with days of catheterization ($r = 0.57$; $p < 0.0001$) and of HPN ($r = 0.61$; $p < 0.000$), whilst it was not related neither with time lasted between CVC implant and HPN initiation, nor with the weekly infusion rate.

The infection rate was higher in patients with a cutaneous stoma ($p = 0.001$), with no differences in the type of infecting agents between patients with or without stoma.

The absolute number of CVC-related bloodstream infections is significantly different ($p < 0.0001$) but, when corrected for the CVC infection rate, the difference is not statistically significant. Finally, there were no differences in the type of infecting agents between oncological and non-oncological patients, as well as, while considering different types of implanted catheters.

4. Discussion

CRBSI is a severe and frequent complication and a common cause of hospitalization for adult patients on HPN [3,9]. The infection rates reported in literature vary from 0.35 to 2.0/1000 days of catheterization, depending on age and type of patients followed, i.e oncological or non-oncological, acute or chronic basic disease, hospitalized or home patients and catheter handling frequency [3,8–15]. Our nutritional team constantly monitored the

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